Results of a Survey of Prothrombin Time Testing Practices in the Pacific Northwest, 2004

Shahram Shahangian, PhD;[1] Kathleen M. LaBeau, MT(ASCP)[2]

[1]Centers for Disease Control and Prevention; [2]Washington State Department of Health

Introduction

Coagulation laboratory tests are known to be vital to diagnosis, treatment and management of bleeding and hypercoagulability disorders. Studies have shown that despite required and voluntary standards of practice, many laboratorians fail to use them.[1] Prothrombin time (PT) is known to be the most commonly performed coagulation laboratory test,[2] and it is now commonly performed using non-traditional test methods [point-of-care (POC) and Clinical Laboratory Improvement Amendments of 1988 (CLIA)-waived test devices]. The devices using such methods differ from traditional laboratory analyzers by using capillary whole blood samples, unitized reagent strips or cartridges, electronic quality control (QC), and pre-set values for international sensitivity index (ISI), for "mean of normal," for reference ("normal") ranges, and for automatically calculated international normalized ratios (INRs). Prothrombin time testing using these devices is common in non-traditional settings (POC and waived test sites) where there is the advantage of the patients being present along with their medical records at the time of testing, and it is increasingly performed by patients themselves using over-the-counter devices. However, such POC testing sites using waived test methods do not have requirements for QC, quality assurance (QA) and personnel qualifications. Many current practice standards and guidelines for PT testing do address these non-traditional test methods.

Purpose of this study. The Washington State Department of Health and the US Centers for Disease Control and Prevention initiated this study of PT testing practices in the US Pacific Northwest (Washington, Oregon, Idaho and Alaska) to

- evaluate current testing practices,
- determine which testing practice standards and guidelines laboratories used, and
- assess why some testing sites do not adhere to accepted standards of practice.

We report practices relating to the PT test including specific QA, test result reporting and competency evaluation practices.

Materials and Methods

Target population. 591 laboratories in the US Pacific Northwest region (Washington, Oregon, Idaho and Alaska) performing the PT test by either waived or non-waived test complexity methods

Questionnaire development. We began the survey process by formulating a set of questions that underwent several revisions to improve clarity, brevity and formatting, and ended the process by pilot testing final versions of the survey using management personnel of 5 coagulation laboratories in the State of Washington.

Data collection. We collected data between January 27, 2004 and March 19, 2004, and sent a reminder postcard to each targeted laboratory, but did not follow up non-responders via telephone.

Data analysis. We excluded all negative responses to a gate question and positive responses to one or more following sub-questions. For yes-or-no questions, percentages are those of affirmative responses; while for multiple-choice questions, percentages relate to proportion of those responding to one or more selections. All *P* values were determined using 2-tailed χ^2 test, and values of <0.05 were considered to demonstrate statistical significance.

Results and Discussion

Response Rate

Of the 591 laboratories targeted, 50% (297) responded. Response rates ranged from 40% in Alaska (42 targeted laboratories) to 56% in Washington (271 targeted laboratories).

Purpose of Performing PT Testing

Of the 297 respondents, PT testing was performed for the following purposes:

- monitoring of oral anticoagulant therapy, 90%,
- evaluation of bleeding, 76%,
- assessment of liver disease, 68%, and/or
- Detection of factor deficiency, 60%.

International Sensitivity Index (ISI) of Thromboplastin Lot

The ISI value of the respondents' current thromboplastin lot ranged from 0.85 to 2.33 (average, 1.41; median, 1.25).

Of the 219 respondents,

- 67% (147) reported ISI values of ≤1.70 (CAP recommends thromboplastins with a manual ISI between 0.90 and 1.70, with a preference towards the lower end of this scale[3]),
- 66% (144) reported ISI values of ≤1.50 [NCCLS (now, Clinical and Laboratory Standards Institute) recommends ISI values of ≤1.50.[4]], and
- 49% (108) reported ISI values of ≤1.20. (American College of Chest Physicians recommends ISI values of ≤1.20.[5])

Optimal ISI has not been rigorously defined by laboratory studies or clinical trials.[3] While sensitive thromboplastin reagents with lower ISI values may offer the potential for improved precision in determining the INR [due to the fact that $INR = (PT\ ratio)^{ISI}$ where PT ratio = patient PT/mean normal PT], some studies have suggested that low-ISI reagents may be less precise.[6]

Sensitivity of PT Assay to Heparin

Of the respondents,

- 12% (29) reported determining sensitivity of their PT assays to heparin, and
- 42% (94) reported selecting a thromboplastin reagent that was insensitive to heparin in the therapeutic range.

According to consensus guidelines developed at the 1997 conference of the CAP, laboratories should determine sensitivity of their PT assay to heparin and, where possible, select a thromboplastin that is insensitive to heparin in the therapeutic range.[3]

Testing Site and Method of Specimen Collection

- 5% (13/259) noted their patients performing any PT test on themselves using a self-testing device,
- 83% (216/260) noted that they collected specimens for PT testing by venipuncture, and
- 87% (71/82) noted that they collected specimens for PT testing by finger stick or capillary collection. Of the 82 respondents, 87% (71) reported having a written policy on the proper collection of capillary specimens.

Use of Sodium Citrate Anticoagulant

Of the 206 respondents collecting specimens by venipuncture,

- 93% (192) used 3.2% (109 mmol/L) sodium citrate as anticoagulant, and
- 5% (10) used 3.8% (129 mmol/L) sodium citrate.

Based on the recommendations made by WHO and NCCLS, 3.2% citrate is the anticoagulant of choice for the coagulation laboratory testing.[3,7] The recommendation to use 3.2%, instead of 3.8%, sodium citrate was supported by noting that the concentration of sodium citrate had a significant effect on PT assay results.[8] Under-filling of specimen tubes containing 3.8% sodium citrate has been observed to prolong PT compared to tubes containing 3.2% sodium citrate.[9]

Specimen Rejection Policies

Of the 230 respondents, 91% (209) reported having a written policy on specimen acceptability.

Specimen Acceptance/Rejection Issues Addressed in Written Policies

Issue	Proportion (Number)
Correct volume of blood	97% (194)
Properly anticoagulated specimen	97% (194)
Appropriate storage temperature	97% (189)
Adequate labeling of specimen	96% (190)
Time delays prior to testing	96% (187)
Adequate centrifugation (speed and time)	92% (178)
Information on requisition and specimen label match	90% (174)
Adequate information on requisition	90% (173)
Hemolysis	89% (170)
Appropriate transport times	89% (168)
Order of multiple tubes	86% (166)
Lipemia	78% (146)
Drawing specimens from patient lines	73% (136)
Icterus	71% (131)
Difficult draws	67% (127)
Collection of samples in a syringe	66% (129)
Abnormal hematocrits	65% (123)
Heparinized specimens	60% (113)

Practices following Implementation of New Thromboplastin Reagents

Given a list of 8 practices associated with validation of new lots of thromboplastin reagents, participants responded affirmatively ranging from 24% for establishing ISI with calibrators to 84% for verifying their reference range:

Practices Followed with Implementation of New Thromboplastin Reagents

Practice	Proportion (Number)
Verify reference ('normal') range	84% (196)
Verify that ISI is correct for instrument/reagent combination	81% (188)
Establish patient mean of normal	80% (183)
Conduct parallel testing between lots	77% (179)
Confirm calculations of INR	75% (173)
Alert clinicians when new reagent/different ISI is used	57% (130)
Perform correlation studies with another method or site	42% (95)
Establish ISI with calibrators	24% (52)

Various practice standards address issues associated with implementing new lots of testing reagents.[3,4,10] Some address general activities such as establishing or verifying patient reference ranges and mean of normal, and some are specific for handling new lots of thromboplastin reagents. Verification of the ISI value in the product insert with every lot of reagents (whether a change is expected or not) is a simple, but effective, solution to help alleviate serious calculation errors.[11] In this survey, of the 231 respondents, 188 (81%) verified that their ISI value is correct for their instrument/reagent combination.

Measurement Unit for PT

Of the respondents,

- 99.6% (232) reported PT as INR,
- 89% (204) reported PT in seconds, and
- 7% (14) reported PT as a therapeutic ratio.

WHO recommends that reporting of PT results for patients on oral anticoagulation therapy include the use of INR values.[12] Other practice standards and publications suggest this as well.[3,4,6]

Items Reported to Clinicians

Of the responders, the following proportions provided the information items below:

Items Provided in the Report to Clinicians

Item	Proportion (Number)
Reference ("normal") range	84% (211)
Specimen comment	79% (195)
Therapeutic range	74% (182)
Result interpretation	30% (66)

The proportion providing any interpretation of PT results provided to the clinician (30%) was significantly greater than the 6% of respondents noting so in the 2001 survey of US hospital coagulation laboratories ($P < .001$).[1]

Repeating a Test

Given a list of 7 items that may prompt repeating a test, participants responded affirmatively ranging from 29% for computer tracking system for monitoring of laboratory services and products to 99% for instrument failure or flag:

Items Prompting a Test Repeat

Practice	Proportion (Number)
Instrument failure or flag	99% (255)
QC value outside of acceptable limits	97% (243)
Critical patient value	95% (244)
Unusual value for patient's history	82% (204)
Abnormal patient value	59% (148)
Information from patient interview	34% (80)
Computer tracking system	29% (69)

Performance of QA Procedures

Given a list of 10 QA procedures, participants responded affirmatively ranging from 32% for monitoring the rate of patient test repeats to 100% for immediately alerting clinicians about critical test results:

Performance of Specific QA Procedures

QA procedure	Proportion (Number)
Immediately alerting clinicians about critical results	100% (254)
Verifying performance of new analytical test systems	95% (225)
Participating in proficiency testing	91% (232)
Assuring clinicians' receipt of patient test results	91% (229)
Periodically verifying calibration of all instrumentation	86% (212)
Comparing instrument print out to reported value	78% (183)
Comparing current and previous values (delta check)	73% (178)
Monitoring rate of critical values reported	45% (109)
Monitoring rate of patient specimen redraws	38% (93)
Monitoring rate of patient test repeats	32% (77)

According to the CLIA regulations, the laboratory must immediately alert the individual or entity requesting the test and, if applicable, the individual responsible for using the test results whenever any test result indicates an imminent life-threatening condition, panic or alert values.[13] The CAP requires laboratories to notify medical staff immediately when a critical value is obtained so that appropriate action can be taken.[14]

According to the CLIA regulations, calibration and calibration verification procedures are required to substantiate the continued accuracy of the test system throughout the laboratory's reportable range of test results.[15] In the current survey, 5% reported not verifying performance of new analytical test systems ($P < .001$), and 14% reported not periodically verifying calibration of all instrumentation ($P < .001$).

Given a list of 6 evaluation activities to assess personnel competency, participants responded affirmatively ranging from 26% for performance in periodic written examinations to 96% for performance of QC:

Evaluation of Personnel Competency

Evaluation activity for personnel competency	Proportion (Number)
Performance of QC	96% (246)
Review of procedure manuals	89% (226)
Direct observation of testing	88% (219)
Participation in continuing education	80% (201)
Analysis of unknown samples	77% (193)
Performance in periodic written examinations	26% (64)

Use of Voluntary Practice Standards

Of those responding, a minority (22%-46%) stated using voluntary practice standards to select their reagents, select citrate concentration, develop policies for specimen acceptability, and develop policies for validating new lots of reagents. Of those not using practice standards, 51%-60% reported not being aware of them. Other most commonly stated reasons for not following voluntary practice standards was performing own studies (25%-31%), performing own literature review (20%-33%), and following manufacturer's recommendation (9%-15%). Of those noting that they used practice standards, 57%-81% noted NCCLS, and 20%-31% named CAP as the most common source of practice standards:

	Voluntary practice standards to select/develop:			
Do you use?	**thromboplastin reagent**	**citrate concentration**	**policy for specimen acceptability**	**policy for validating new reagent lots**
Yes	22% (53)	39% (82)	46% (94)	33% (81)
No	39% (96)	31% (64)	27% (56)	37% (91)
Do not know	39% (95)	30% (63)	27% (55)	30% (72)
Source of standard				
NCCLS	57% (29)	81% (63)	72% (66)	58% (46)
CAP	31% (16)	31% (24)	20% (18)	30% (24)
Both NCCLS and CAP	18% (9)	24% (19)	14% (13)	18% (14)
Reason not using standard				
Not aware	54% (49)	52% (32)	54% (28)	61% (53)
Perform own studies	27% (24)	33% (20)	31% (16)	28% (24)
Perform own review	23% (21)	25% (15)	25% (13)	20 % (17)

Concluding Remarks

Since the publication of the Institute of Medicine's report in 2000,[16] awareness of preventable medical errors has increased, leading to efforts to create systems that will help detect and eliminate them. An area that has a great potential impact on patient safety is coagulation laboratory testing, and especially the PT test since it is used to monitor oral anticoagulant therapy. For improving the safety of patients undergoing oral anticoagulant therapy, it is necessary first to assess the extent to which hospital laboratories adhere to accepted testing practices. Our results here indicate that many laboratories do not follow certain testing guidelines. Variations in some such practices could have a direct impact on clinical outcomes. Our results show substantial variabilities in some PT testing practices. To evaluate whether laboratories followed accepted standards of laboratory practice, we posed several multiple-choice questions to the survey participants. The findings demonstrate that a large proportion of laboratories either did not follow some current standards/guidelines or were not aware of them. Lack of awareness of published practice guidelines was the major reason for not following them; in this survey, 51%-60% of participants not using accepted standards of practice reported that they were not aware of them. These findings suggest a need for timely interventions to raise awareness of these guidelines for use by medical and health practitioners in the field.